REMARKS

Entry of the foregoing, reexamination and further and favorable reconsideration of the subject application in light of the following remarks, pursuant to and consistent with 37 C.F.R. § 1.112, are respectfully requested.

By the foregoing amendment, claim 14 has been canceled without prejudice or disclaimer of the subject matter recited therein. Claims 10-13 and 15 have been amended to further clarify Applicant's invention. Support for the amendments can be found throughout the specification. Accordingly, no new matter has been added.

Turning now to the Official Action, the drawings have been objected to for the reasons set forth on the PTO-948 form. Enclosed herewith is a Request for Approval of Drawing Changes and upon receipt of such approval, these changes will be implemented through submitted formal drawings.

I. Verified Statement

Applicants submit herewith a Verified Statement pursuant to 37 C.F.R. § 1.804 indicating that the hybridoma cell lines designated in the specification as FERM P-14878, FERM P-14879 and FERM P-14880 have been deposited in accordance with the provisions of the Budapest Treaty. The Verified Statement being submitted herewith is a copy of the Verified Statement filed and accepted in the parent application (Application Serial No. 08/913,315, now U.S. Patent No. 6,015,680) on February 26, 1999.

II. Rejections Under 35 U.S.C. § 112, second paragraph

Claims 10-15 have been rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which applicants regard as the invention. Applicants respectfully traverse this rejection.

Claim 10 is allegedly indefinite for reciting "(SDS-PAGE)" instead of "SDS-PAGE," and for reciting "a molecular weight of 200kD or more" without indicating if the molecular weight was determined under reducing or non-reducing conditions. This rejection is rendered moot in light of the amendments to claim 10. Specifically, claim 10 has been amended to recite "SDS-PAGE" instead of "(SDS-PAGE)," and claim 10 has been amended to recite that the molecular weight was determined under reducing conditions. It is noted that none of these amendments are intended to narrow the scope of any element of claim 10.

Claim 14 is allegedly indefinite for not reciting the depository accession numbers for the claimed antibodies. This rejection is rendered moot in light of the cancellation of claim 14.

In view of the above, applicants respectfully request withdrawal of the rejection of claims 10-15 under 35 U.S.C. § 112, second paragraph.

III. Rejections Under 35 U.S.C. § 112, first paragraph

Claim 14 has been rejected under 35 U.S.C. § 112, first paragraph, as allegedly containing subject matter which was not described in the specification in a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Applicants respectfully traverse this rejection. However, to

expedite prosecution in the subject application and not acquiesce to the Examiner's rejection, claim 14 has been canceled thereby rendering such rejection moot.

Accordingly, applicants respectfully request withdrawal of the rejection of claim 14 under 35 U.S.C. § 112, first paragraph.

To the extent this rejection may be applicable to any of the currently pending claims, as described above, a copy of the Verified Statement filed in the parent application if enclosed herewith.

IV. Rejections Under 35 U.S.C. § 102

Claims 10-12 have been rejected under 35 U.S.C. § 102 as allegedly being anticipated by either Yang et al. (*Am. J. Respir. Cell Mol. Biol.*, 7:161-71, 1992) or Ten et al. (*Anticancer Research*, 6:983-8, 1986). Applicants respectfully traverse this rejection.

It is well settled law that to anticipate a claim, a single reference must teach each and every element of the claim, and the single reference must be enabling. *See Hybritech Inc. v. Monoclonal Antibodies, Inc.*, 802F.2d 1367, 1379, 231 U.S.P.Q. 81, 90 (Fed. Cir. 1986); *Atlas Powder Co. v. E.I du Pont De Nemours & Co.*, 750 F.2d 1569, 1574, 224 U.S.P.Q. 409, 411 (Fed. Cir. 1984).

The Examiner has stated that Yang et al. discloses a glycoprotein molecule of about 200kD which is synthesized by lung adenocarcinoma cells and a method of assaying for these antigens, and that Ten et al. discloses adenosine deaminase complexing protein (ADCP) as a dimeric glycoprotein of 200kD which is decreased in cancers of the lung. While

acknowledging that neither reference discloses the reactivity of the synthesized glocoprotein molecules with the specific lectins MAA or PNA, the Examiner has further stated that the claimed glycoproteins appear to be the same as the prior art glycoproteins, and therefore, would have the same properties of binding to the lectins MAA and PNA.

Applicants submit that Yang et al. fails to teach, either explicitly or inherently, each and every element of the claimed invention. Specifically, Yang et al. fail to teach that the 200kD protein binds to a monoclonal antibody produced by a hybridoma selected from the group consisting of FERM BP-5383, FERM P-14879 and FERM P-14880.

The glycoprotein of the present invention is detectable in the culture broth of lung adenocarcnoma cells and in the sera from lung adenocarcinoma patients, but the glycoprotein is hardly detectable in normal human sera. See page 2, line 20 to page 3, line 6 of the specification. Ten et al., on the other hand, discloses in the introduction that "[t]he normal human prostate, kidney, intestine, liver, lung and primary skin fibroblasts are among the highest expressors of ADCP. It was found that the ADCP expression was markedly decreased or completely absent in the cytosols of a number of *in vitro* transformed skin fibroblasts and in certain cancer derived cells. Earlier studies indicated a sever decrease or deficiency of ADCP also in a number of primary carcinomas of lung . . . ."

Further, the ADCP protein of Ten et al. consist of two identical subunits of about 100kD each and these individual proteins can bind ADA-S to form a molecule of abut 280kD. The protein of the invention has a molecular weight of 200kD or more by SDS-PAGE under reducing conditions. Under SDS-PAGE reducing conditions, the ADCP of Ten et al. would

separate into its individual components of 100kD each. Therefore, the ADCP protein of Ten et al. and the 200kD protein of the invention are clearly different.

Furthermore, like Yang et al., Ten et al. fails to teach that the 200kD protein binds to a monoclonal antibody produced by a hybridoma selected from the group consisting of FERM BP-5383, FERM P-14879 and FERM P-14880.

Therefore, because neither reference teaches, either explicitly or inherently, each and every element of the claimed invention, applicants respectfully request withdrawal of the rejection of claims 10-12 under 35 U.S.C. § 102(b).

Claims 10-12 have also been rejected under 35 U.S.C. § 102 as allegedly being anticipated by either Werner et al. (*Path. Res. Pract.*, 187:864-70, 1991) or Eskelinen et al. (*Anticancer Research*, 14:699-703, 1994). Applicants respectfully traverse this rejection.

The Examiner has stated that Werner et al. discloses the TAG-12 expressed by lung adenocarcinomas with a molecular weight of about 200kD, and a method of detecting lung adenocarcinoma. The Examiner has further stated that Eskelinen et al. discloses that the TAG-12 antigen is secreted.

Applicants submit that neither reference teaches, either explicitly or inherently, each and every element of the claimed invention, and neither reference is enabling. Specifically, the references fail to teach that the 200kD protein binds to a monoclonal antibody produced by a hybridoma selected from the group consisting of FERM BP-5383, FERM P-14879 and FERM P-14880.

Werner et al. teaches that the TAG-12 protein is not secreted. In the introduction, it is stated that "[i]n tissue sections of different breast carcinoma types strong cytoplasmic and

cell membrane staining of tumor cells was observed with 7A9 in more than 95% of the cases." The Examiner relies on Eskelinen to state that TAG-12 is secreted in breast cancer cells, however, there is no teaching that TAG-12 is secreted in lung adenocarcinomas. Further, Eskelinen et al. teaches that none of the serum markers (TPA, TPS, TAG-12, CA 15-3 and MCA) were significant predictors in breast cancer diagnosis. See page 700, column 2, end of Results section. Thus, upon reading these references, the skilled artisan is not taught that TAG-12 is secreted in lung adenocarcinomas, and the skilled artisan is taught that TAG-12 is not a significant predictor in breast cancer diagnosis.

Therefore, because neither reference teaches, either explicitly or inherently, each and every element of the claimed invention, applicants respectfully request withdrawal of the rejection of claims 10-12 under 35 U.S.C. § 102(b).

Claims 10-13 have been rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Taniguichi et al. (EP 0232871A). Applicants respectfully traverse this rejection.

The Examiner has stated that Taniguichi et al. discloses a 200kD antigen secreted by lung adenocarcinoma and a method for detecting lung squamous cell carcinoma. Like the protein of Ten et al., this protein has a molecular weight of 200kD by SDS-PAGE under non-reducing conditions. Under reducing conditions, however, the protein is separated into approximately 3 subunits with a molecular weight of 65kD. See Figure 2, and page 6, lines 41-44 of Taniguichi et al. The protein of the present invention has a molecular weight of 200kD under reducing conditions. Further, the protein of Taniguichi et al. is not secreted.

Rather, page 6, lines 41-42 state that the 200kD protein is from the soluble fraction on the surface of cellular membranes of PC10 cells.

Therefore, because Taniguichi et al. fails to teach, either explicitly or inherently, each and every element of the claimed invention, applicants respectfully request withdrawal of the rejection of claims 10-13 under 35 U.S.C. § 102(b).

V. Rejections Under 35 U.S.C. § 103

10-12 and 15 have been rejected under 35 U.S.C. 103(a) as allegedly being unpatentable over Taniguchi et al. (EP 0232871A) in light of Wright (U.S. Patent No. 5,314,996). Applicants respectfully traverse this rejection.

In proceedings before the Patent and Trademark Office, the Examiner bears the burden of establishing a *prima facie* case of obviousness based upon the prior art. The Examiner can satisfy this burden by showing, first, that the cited prior art coupled with the general knowledge at the time of the invention must contain some suggestion or incentive to motivate a skilled artisan to modify or combine references. *See In re Fine,* 837 F.2d 1071, 1074, 5 U.S.P.Q.2d 1596, 1598 (Fed. Cir. 1988); *In re Skinner*, 2 U.S.P.Q.2d 1788, 1790 (Bd. Pat. App. & Int. 1986). Second, the Examiner must show that the modification or combination of prior art references must have a reasonable expectation of success (at the time of the invention). *See Amgen, Inc. v. Chugai Pharm. Co.*, 927 F.2d 1200, 1209, 18 U.S.P.Q.2d 1016, 1023 (Fed. Cir. 1991). Lastly, the Examiner must show that the cited or combined references teach each and every limitation of the claims. *See In re Zurko,* 111 F.3d 887, 888-89, 42

U.S.P.Q.2d 1476, 1478 (Fed. Cir. 1997); *In re Wilson,* 424 F.2d 1382, 1385, 165 U.S.P.Q. 494, 496 (C.C.P.A. 1970).

The remarks regarding Taniguichi et al. above are incorporated herein by reference. The Wright patent fails to remedy the serious deficiencies of Taniguichi et al. In particular, neither Wright nor Taniguichi et al. teaches a glycoprotein with a molecular weight of 200kD by SDS-PAGE under reducing conditions or a glycoprotein that is secreted from lung adenocarcinoma cells.

The Examiner relies upon the Wright patent for teaching a method of detecting prostate carcinoma. However, since neither reference, either alone or in combination, teach or suggest the particular glycoprotein antigen as claimed, a proper case of *prima facie* obviousness has not been established.

Therefore, applicants respectfully request withdrawal of the rejection of claims 10-12 and 15 under 35 U.S.C. § 103(a).

VI. Double Patenting Rejection

Claims 12-15 have been rejected under the judicially created doctrine of obviousness-type double patenting as allegedly being unpatentable over claims 4-8 of U.S. Patent No. 6,015,680. This rejection is respectfully traversed. However, to expedite prosecution in the subject application and not to acquiesce to the Examiner's rejection, applicants submit herewith a terminal disclaimer in compliance with 37 C.F.R. 1.321(c).

In view of the foregoing, further and favorable action in the form of a Notice of Allowance is believed to be next in order. Such action is earnestly solicited.

In the event that there are any questions relating to this application, it would be appreciated if the Examiner would telephone the undersigned agent concerning such questions so that prosecution of this application may be expedited.

Respectfully submitted,

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Date: March 2, 2001

Attachment to Amendment and Reply dated March 2, 2001

Marked-up claims 10-13 and 15

10. (Amended) A glycoprotein antigen having a molecular weight of 200 kD or more as determined by [(]SDS-PAGE[),] under reducing conditions, which is expressed by cells of human lung adenocarcinoma, and is secreted by said lung adenocarcinoma, wherein said glycoprotein antigen specifically binds to a monoclonal antibody produced by a hybridoma selected from the group consisting of FERM BP-5383, FERM P-14879 and FERM P-14880.

11. (Amended) The glycoprotein antigen according to Claim 10, wherein [it] said glycoprotein antigen reacts with MAA lectin and PNA lectin but does not react with GNA lectin, SNA lectin, and DSA lectin.

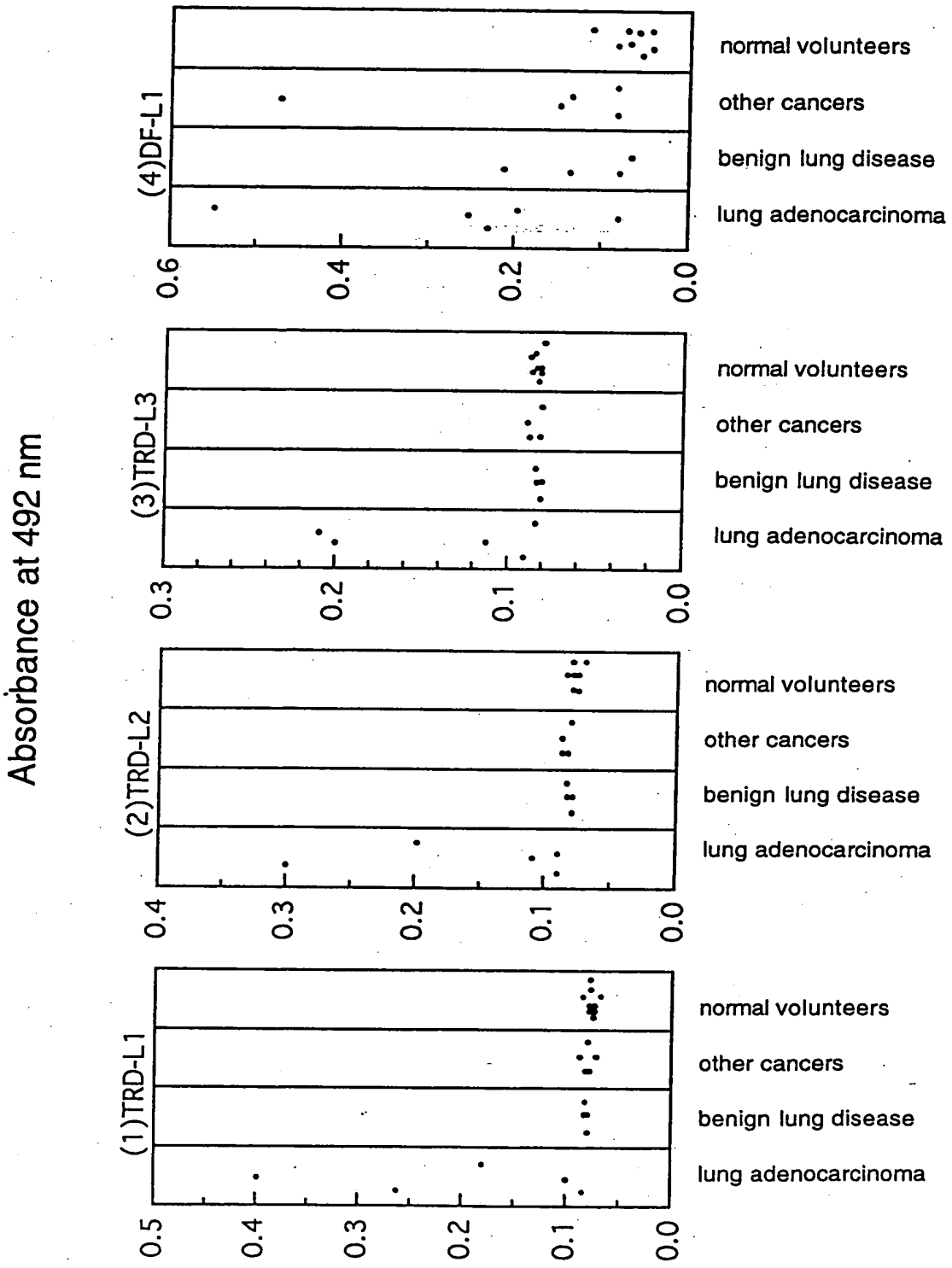
12. (Amended) An immunoassay method for diagnosis of human lung adenocarcinoma which comprises contacting a sample suspected of containing human lung adenocarcinoma cells with a diagnostically effective amount of [a] said monoclonal antibody or a fragment thereof of claim 10 [which specifically binds to the glycoprotein antigen of Claim 10], and determining whether said sample contains human adenocarcinoma cells based on the binding or absence of binding of the glycoprotein antigen in said sample to said monoclonal antibody.

13. (Amended) [An] The immunoassay method according to Claim 12, wherein the isotype of said monoclonal antibody is IgM.

15. (Amended) [An] The immunoassay method according to Claim 12, wherein said antibody is a Fab, $F(ab)_2$ or Fv fragment.

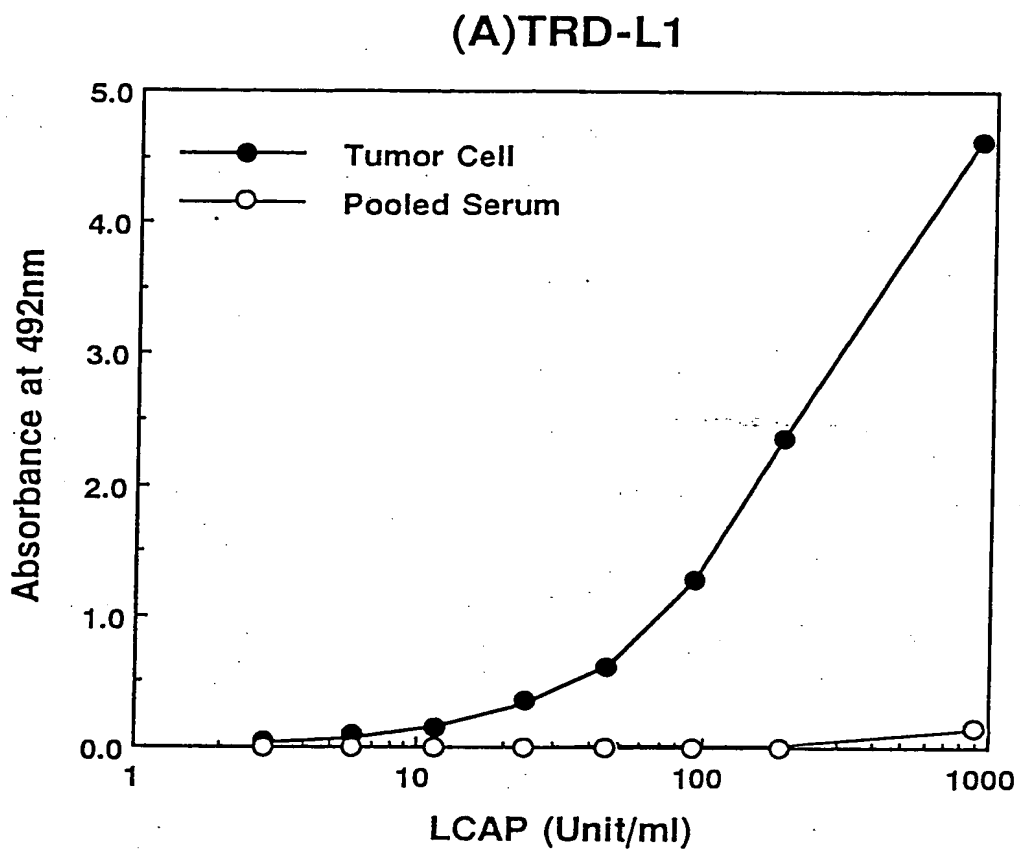
~~FIG. 2~~

FIG. 2


Absorbance at 492 nm
(4)DF-L1
0.6
0.4
0.2
0.0
normal volunteers
other cancers
benign lung disease
lung adenocarcinoma
(3)TRD-L3
0.3
0.2
0.1
0.0
normal volunteers
other cancers
benign lung disease
lung adenocarcinoma
(2)TRD-L2
0.4
0.3
0.2
0.1
0.0
normal volunteers
other cancers
benign lung disease
lung adenocarcinoma
(1)TRD-L1
0.5
0.4
0.3
0.2
0.1
0.0
normal volunteers
other cancers
benign lung disease
lung adenocarcinoma

~~FIG. 3~~

FIG 3


(A)TRD-L1
Tumor Cell
Pooled Serum
Absorbance at 492nm
5.0
4.0
3.0
2.0
1.0
0.0
1
10
100
1000
LCAP (Unit/ml)

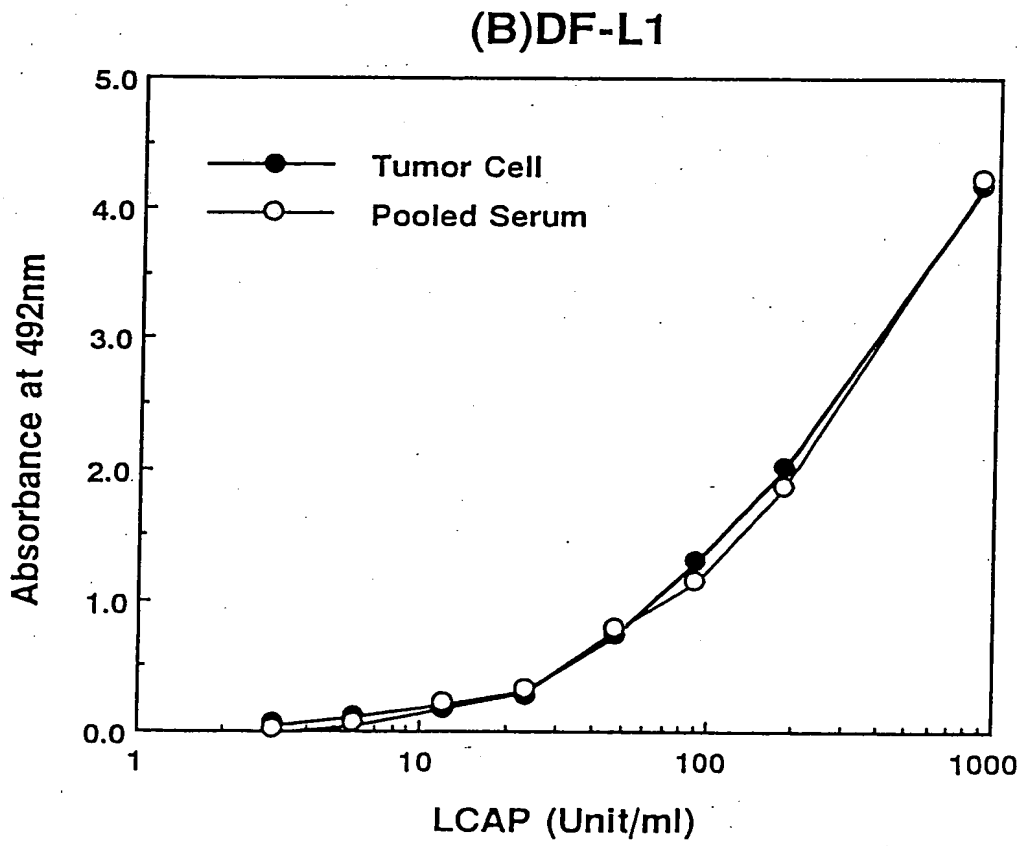
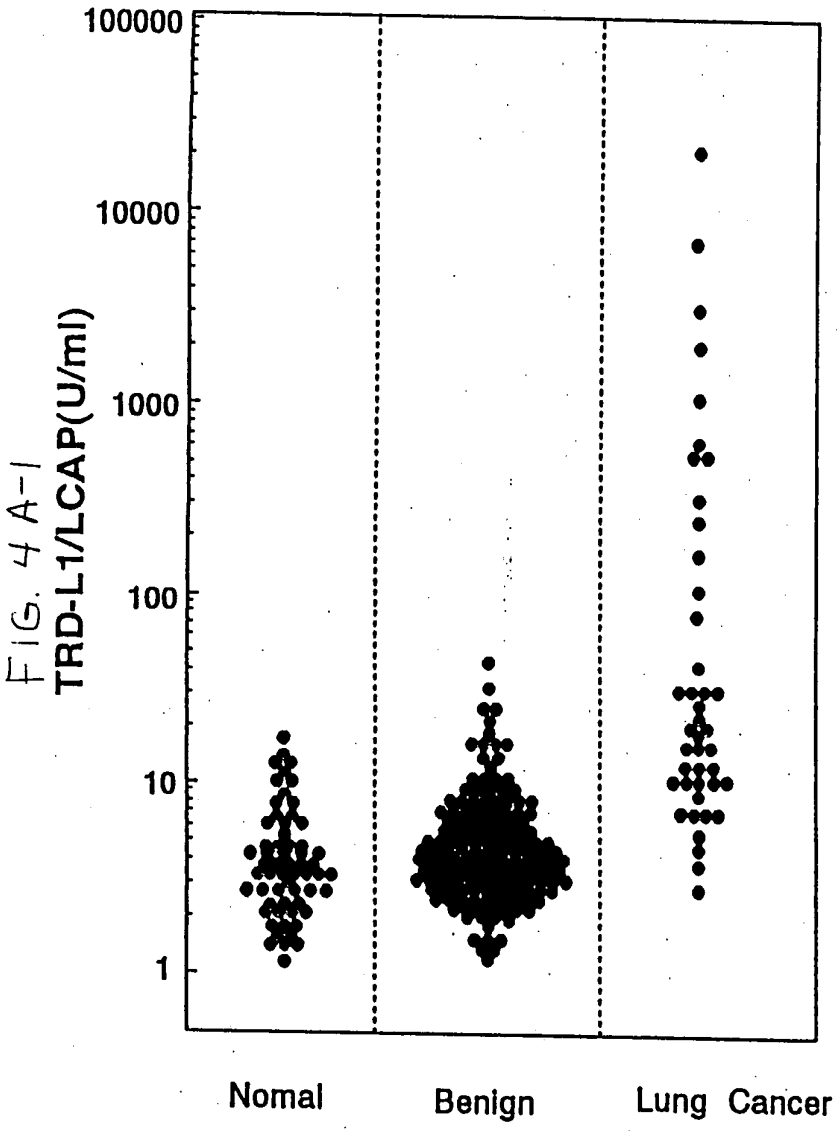
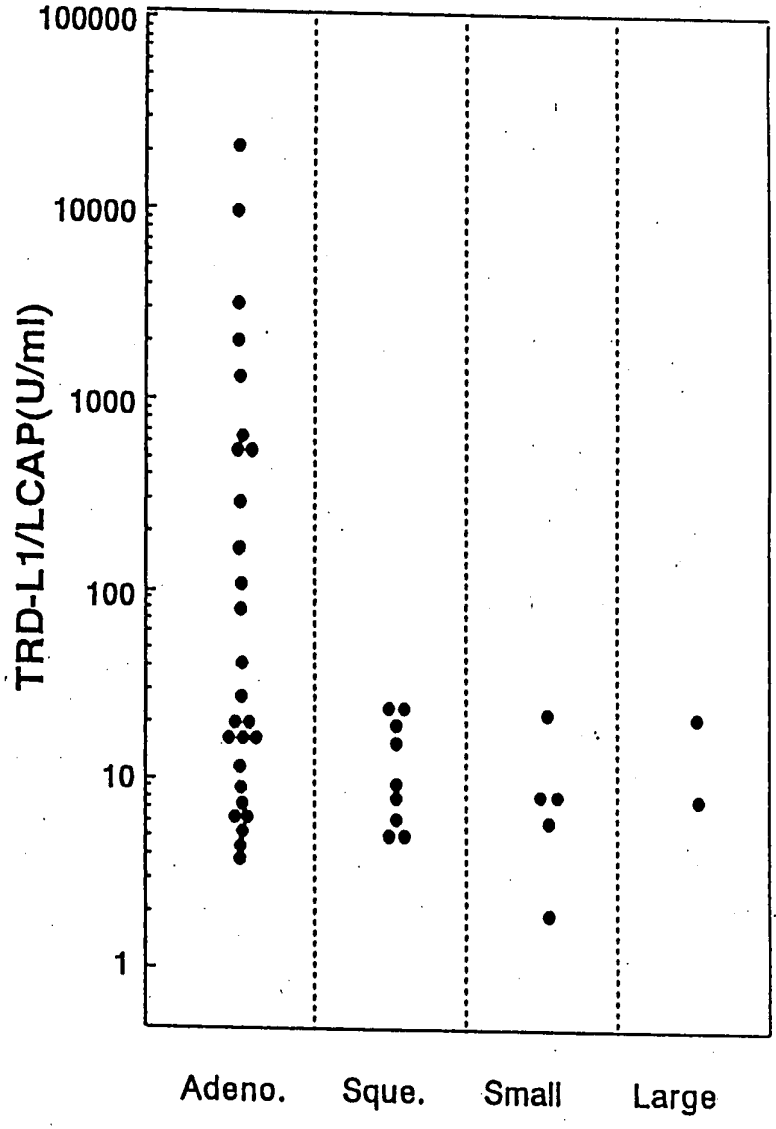

(B)DF-L1
Tumor Cell
Pooled Serum
Absorbance at 492nm
5.0
4.0
3.0
2.0
1.0
0.0
1
10
100
1000
LCAP (Unit/ml)

FIG. 4 A-1



(A) Lung Disease



(B) Lung Cancer